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THE DIAGNOSTIC VALUE OF THE VARIATIONS
IN THE LEUCOCYTES AND OTHER BLOOD CHANGES
in Typhoid and Malarial Remittent Fevers
Respectively.

L. Rogers.

British Medical Journal, 1902, i.

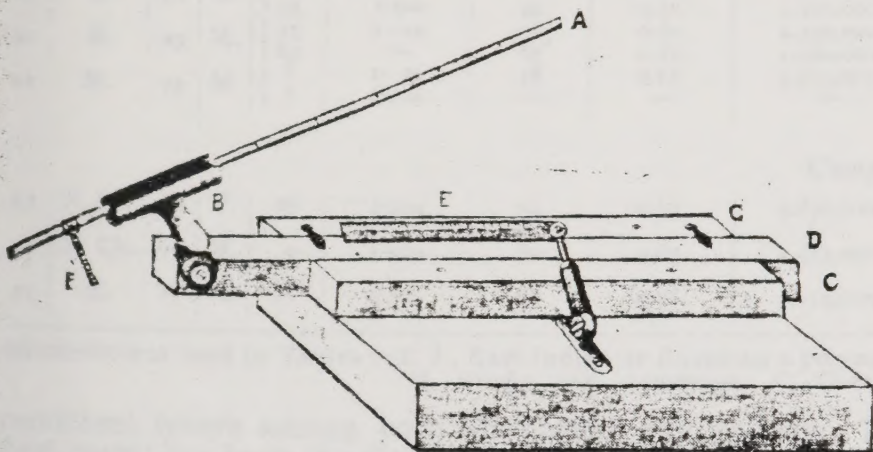


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left standing at a desired temperature, the rate of precipitum formation, etc., being noted.

After twenty-four hours have elapsed, the precipitum has become deposited upon the bottom of the tube. Should any adhere to the walls of the vessel, it may be dislodged by gently tapping or rotating the tube upon its vertical axis. The particles thus displaced soon sink to the bottom of the tube, provided it does not contain too much serum, which through its viscosity impeded their gravitation. The clear supernatant fluid is now pipetted off by means of a conveniently bent bulbed capillary pipette, the tip of which is allowed to slide down along the inner wall of the test tube, the precipitum not being disturbed, the clear fluid being aspirated into the bulb as the tip of the pipette slides down a little beneath the receding surface of the column of fluid in the tube. The bulk of precipitum and clear fluid left is so small that it can now be readily drawn up into the capillaries.

The capillaries used for measuring the precipitum volumetrically are made of fairly thick glass, are about 12 cm. long, and have a lumen of about 1 mm. The ends should be cut off square by means of a diamond, this being essential, as it is thus possible to practically remove all the fluid and precipitum in the bottom of the small test tube. The end of the capillary is placed against the bottom of the tube, and the deposit and fluid are well mixed by being drawn backwards and forwards into the capillary. It is imperative that bubbles should be avoided. The fluid is now drawn up a little way into the capillary, and the end of this is drawn out and sealed in a very small flame. The sealed end should be blunt to avoid possibility of breakage; the other end of the tube, which can now be cut down to a convenient length, is left open. After a number of capillaries have been thus prepared, they are placed vertically in a cool place. After twenty-four hours the height of the column of precipitum is marked upon the capillary with a glass pencil. After forty-eight to seventy-two hours it will be seen that the column of precipitum remains constant. The amount of precipitum may now be measured.



The accompanying figure shows a little apparatus which I have made in the laboratory, and have found very convenient for making these measurements of the amount of precipitum. A fairly large thermometer tube (A) is used which is graduated in tenths of a c.c.m., the calibre being chosen so that a fine steel scale of 10 cm. (E) subdivided into 0.5 mm. corresponds to the length of column of fluid measuring 0.1 c.c.m. in the tube. The tube is filled with pure water up to the graduation mark, the mouth being wiped dry with filter paper. The tube is fixed in a spring clip which is attached to the wooden rod (D) so that it pivots in a vertical plane, thus permitting the tube to rest in a horizontal position or at any desired angle. The rod (D) slides horizontally between the rods C and C', which are nailed to a solid block of wood beneath. Two small brass plates attached to rod C prevent rod D from being displaced. The steel cm. measure is attached to a metal support, which is screwed to the block beneath. By a lucky chance I happened to have an old "peep sight" from a sporting rifle which served admirably for carrying the metal scale, as it can be inclined at any angle and be screwed up or down. By pivoting the scale on a screw passing through the eyehole of the sight, the scale can be placed and retained at any angle on its support, thus making it possible to closely apply the fine scale to the thermometer tube in any position desired.

The height of the volume of precipitum having been marked upon the capillary tube, the latter is cut square by means of a diamond at the lower meniscus, a small quantity of air having been left in the lower end of the tube when it was sealed. The contents of the tube are blown out, the tube is drained as far as possible by blowing out the moisture it contains on to filter paper, or it can be washed out and dried. The mouth of the capillary is now brought in contact with the end of the thermometer tube, which has been slightly raised at one end (A), and fluid is allowed to pass into the capillary up to the pencil mark previously noted. The amount of fluid which has passed into the capillary is now read off on the scale. The thermometer tube is moved by means of the handle (F) so as to prevent expansion of the fluid through the heat of the hand. Where it is desired to know the actual quantity of precipitum, it is necessary to note the temperature and calculate accordingly. This may be disregarded when a simple comparison is being made with different quantities of precipitum in a given series, the measurements being made in rapid succession under similar outward conditions. If it is desired to make simply comparative measurements a diamond scratch on any suitable tube is sufficient, only the measurements on the steel scale being recorded.

I am at present engaged, with the aid of Mr. T. Strangeways-Pigg, in making measurements of the degree of reaction, etc., by means of this method, and we shall very shortly report upon our results, which are certainly striking. We hope to succeed in standardizing our antiserum by this method.

I have described my method thus in detail, so as to give

others an early opportunity of putting it to the test. We have so far obtained what appear to be remarkable results. If we count the amount of precipitum, measuring about 0.03 c.c.m., obtained from adding 0.1 c.c.m. of an antiserum to 0.5 c.c.m. of its homologous dilution (1 to 100 or 1 to 200) as 100, then we obtain figures somewhat as follows:

Antisheep Serum.					Antipig Serum.				
Sheep ...	...	...	...	100	Pig ...	...	...	...	100
Ox ...	...	...	...	80	Horse ...	...	...	...	16
Antelope ...	...	...	...	50	Hog deer ...	...	...	...	14
Hog Deer ...	...	...	...	47	Cat ...	...	...	...	14
Reindeer ...	...	...	...	30	Dog ...	...	...	...	13
Pig ...	...	...	...	20	Sheep ...	...	...	...	13
Horse ...	...	...	...	16	Wallaby ...	...	...	...	5
Cat ...	...	...	...	12					
Dog ...	...	...	...	7					
Wallaby ...	...	...	...	5					

In both series we observe the occurrence of what I have termed the mammalian reaction, both antisera being very powerful. I do not wish these numbers to be taken as final, nevertheless they very definitely show that the results which I have published, based upon cruder methods of experimentation, are essentially correct. To obtain a constant it will be necessary to make repeated tests with the bloods of each species and with different antisera of one kind, making the tests with different dilutions and different proportions of antiserum. I am inclined to believe that with care we shall perhaps be able to "measure species" by this method, for it appears from the above results that there are measurable differences in the reactions obtained from related bloods, in other words, determinable degrees of blood relationship which we may be able to formulate.

NOTES.

¹ BRITISH MEDICAL JOURNAL, May 11th, 1901, vol. i, p. 1141; September 1st, vol. ii, p. 669; *Journ. of Hygiene*, July 1st, 1901, vol. i, pp. 367-387; *Proc. Roy. Soc.*, vol. lxxix, pp. 150-153 (paper read November 21st); *Journ. Trop. Med.*, December 16th, 1901, pp. 405-408; *American Naturalist*, vol. xxxv, pp. 927-932; *Proc. Phil. Soc.*, Cambridge meeting of January 20th, 1902.
² In 2 instances out of 510 tests a faint clouding was observed to take place in a dilution of avian blood, tested by means of an antimammalian serum and vice versa. In both cases the blood samples had been collected with other bloods. In one case I received samples of avian and mammalian bloods collected on the same day by a sportsman, and I have no doubt but that the filter-paper strips came in contact with each other in a moist state, a possibility against which I have sounded a warning in my circular letter. As I was the first to show, these reactions come off, even in mixtures of several kinds of blood. Such accidents can be prevented by the use of paraffined envelopes, which I have sent out with my blood-collecting "outfit."

THE DIAGNOSTIC VALUE OF THE VARIATIONS IN THE LEUCOCYTES AND OTHER BLOOD CHANGES

IN TYPHOID AND MALARIAL REMITTENT FEVERS RESPECTIVELY.

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DURING the last few years much attention has been paid to the blood changes in the specific fevers, and the great diagnostic value, especially of the variations in the numbers, of both the total and individual leucocytes has been fully recognized. At the same time the discovery of the serum test for typhoid and Malta fevers and the great progress in our knowledge of malarial parasites has placed in our hands valuable aids in the differentiation of the still far too little known tropical fevers.*

Recently, through the kindness of the medical officers in charge of the different Calcutta hospitals, I have been able to study the blood changes in some fifty cases of continued and

* More than four years ago I made arrangements for applying these modern methods to the study of fevers in a large military station in India, but at a day's notice was whisked off to a frontier expedition, and until a few months ago was prevented by the exigencies of military and special duty from pursuing this interesting field of study, a fact which I only mention because too little allowance is made for the difficulties and interruptions of scientific work in India by those who criticize the paucity of results obtained in this country.

TABLE I.

Number of Case.	Nationality.	Age.	Sex.	Day of Disease.	Dilution of Serum with Typhoid Reaction.	Percentage of Haemoglobin.	Haemoglobin Value or Colour Index.	Red Corpuscles per Cubic Millimetre.	White Corpuscles per Cubic Millimetre.	Ratio of Red to White Corpuscles.	Percentage of Polynuclears.	Lymphocytes.	Large Mononuclears.	Remarks.
1	E. I.	15	F.	7	1-100	72	0.75	4,790,000	4,375	1-1095	65.0	31.4	2.8	Average severity.
				16	—	59	0.77	3,855,000	4,000	1-964	55.0	42.0	3.0	
				25	1-500	68	0.81	4,185,000	5,500	1-761	47.6	48.6	3.6	
2	E.	22	M.	10	1-100	78	0.75	5,190,000	4,500	1-1153	59.0	38.2	2.8	Severe.
				30	1-200	69	0.77	4,450,000	9,500	1-467	47.0	50.0	2.4	
3	N. Ch.	14	F.	20	1-100	63	0.73	4,320,000	7,500	1-576	58.2	35.4	6.4	Severe.
4	N. Ch.	16	F.	14	1-40	58	0.80	3,620,000	1,250	1-2896	51.0	43.3	4.7	Mild.
				25	1-100	59	0.73	4,010,000	1,250	1-3208	48.6	41.8	5.2	
5	M.	23	M.	20	1-100	78	0.70	5,530,000	6,250	1-885	73.4	22.0	4.0	Severe; no fever 6 days.
				44	—	60	0.60	4,480,000	4,500	1-1106	49.8	46.2	2.2	
6	M.	20	M.	17	1-500	67	0.75	4,465,000	2,500	1-1786	45.6	49.0	4.2	No fever 14 days.
				35	—	—	—	—	—	—	61.6	33.6	4.4	
7	H.	30	M.	23	1-100	71	0.68	5,255,000	6,625	1-793	47.6	47.8	4.4	Relapse.
				66	1-500	—	—	—	—	—	53.2	42.4	4.2	
8	H.	20	M.	17	1-20	46	0.66	3,460,000	1,750	1-1977	52.0	40.5	6.0	Previous malaria.
				24	—	44	0.68	3,220,000	3,625	1-888	54.5	39.5	5.5	
9	Ar.	14	F.	14	1-100	55	0.63	4,375,000	4,875	1-897	44.8	48.8	5.6	Mild.
10	C.	26	M.	23	1-40	51	0.75	3,380,000	3,125	1-1082	50.0	45.5	4.5	
				33	1-100	49	0.70	3,500,000	3,250	1-1076	68.0	34.0	3.6	Mild; no fever 3 days.
11	G.	25	M.	35	1-40	56	0.62	4,550,000	3,500	1-1300	46.0	46.0	—	
				85	—	67	0.73	4,590,000	6,000	1-765	51.0	42.8	5.2	Severe, with relapse.
12	H.	23	M.	?	1-20	48	0.61	3,915,000	4,875	1-803	37.8	57.6	4.4	
				?	1-100	—	—	—	—	—	45.2	48.2	6.6	Admitted in relapse.
Complicated Cases.														
13	N. Ch.	8	F.	26	1-100	54	0.70	3,850,000	6,250	1-786	87.6	8.8	3.2	Local peritonitis.
14	N. Ch.	12	M.	9	1-500	62	0.63	4,945,000	5,500	1-829	79.4	17.6	2.4	Ditto.
15	H.	27	M.	18	1-100	80	0.78	5,115,000	10,125	1-505	81.0	15.4	3.2	Pneumonia.

Abbreviations used in Tables:—E. I., East Indian or Eurasian a person of mixed blood. E., European. N. Ch., Native Christian. M., Mohammedan. H., Hindu. Ar., Armenian. C., Chinaman. G., Goanese. M. T., Malignant Tertian.

remittent fevers among both Europeans and natives. The first result has been the discovery that typhoid fever is really quite common among natives of India, and they are very far from presenting any degree of immunity from the disease as held by at least one recent writer,¹ but this part of the subject I have already dealt with in another place.² Further, it has been found that the alterations in the blood which take place during attacks of typhoid and malarial remittent fevers respectively differ in certain important respects, and that these differences are sufficiently definite and constant to be of diagnostic value, while they are so easily tested as to be of practical use; and it is with this part of the subject that I propose to deal in the present paper.

In India, and probably also in many other tropical climates, by far the commonest fevers, and in their earlier stages, at any rate, the most frequently confused continued and remittent are typhoid and the severer forms of malaria. The latter frequently do not come under observation until after they have been liberally dosed with quinine, as a consequence of which parasites are often absent from the peripheral circulation, while it has recently been shown³ that they may not be found after long and repeated search, even when no quinine has been taken. Moreover, facilities for carrying out Widal's test for the former fever are only too often not available in tropical stations. Any easily detected blood change which will differentiate between these two forms of fever may, then, be of the utmost practical value. Such, I believe, we have in the variations in the proportions of the different kinds of leucocytes. It has long been known that the total leucocyte count is decreased in both typhoid and malarial fevers, this change often being very marked in malarial cases as I show elsewhere.⁴ More recently it has been pointed out by Drs. Stephens and Christophers of the Royal Society's Malaria Commission⁵ that the percentage of large mononuclear white corpuscles is considerably increased in malarial fevers, this change being most marked during the intermissions or remissions of the fever, and the counts recorded by Turk⁶ confirm this observation. In typhoid, on the other hand, the last named observer gives figures showing an increase in the lymphocytes as the most marked

change, the large mononuclears showing no increase, although Cabot says these last are also increased in typhoid.

The question, then, arises whether these differences in the two forms of fever are sufficiently constant and marked to be of diagnostic value, and whether there are any other changes in the blood which may be of service in the same way. In order to test this a series of cases of both forms of fevers have been submitted to the following examination. The percentage of haemoglobin and the number of red and white corpuscles respectively per cubic millimetre have been estimated with Gowers's instruments. From the first two data the haemoglobin value or amount of haemoglobin in each red corpuscle compared to unity is obtained, and from the last two the proportion of white to red corpuscles is worked out. The percentage of the different forms of leucocytes is estimated from a count of 500 in a blood slide stained by Romanowsky's method, this being also used for searching for malarial parasites. Lastly, every case has been examined for Widal's serum reaction for typhoid fever, and most of them also for Malta fever, although the latter has invariably given negative results. Four-hour temperature charts and clinical notes have also been obtained from the hospital records.

THE BLOOD CHANGES IN TYPHOID FEVER.

In Table I the results of the blood examinations in a series of cases of typhoid fever are given, and can be contrasted with those of another series of malarial remittent fevers, which are recorded in Table II. The nationality, age, and sex are also given, the day of the disease when the blood was examined, and the highest dilution in which the serum gave a complete agglutination reaction with a one-day broth culture within one hour, this having been tested in each case in dilutions of 1 in 20, 1 in 40, and 1 in 100, and sometimes in higher ones. Cases with complications are placed at the end of the table. The cases are a consecutive series, although they have been arranged in accordance with the day of the disease when first examined, beginning with the earliest dates. Nearly as many more cases might have been given, but they show precisely similar results, and the general features are so constant that those revealed afford sufficient data for comparison with the malarial series in Table II.

TABLE II.

Number.	Nation-ality.	Age.	Sex.	Tempera- ture when Blood was Taken.	Highest Tempera- ture Previous Evening.	Percentage of Haemo- globin.	Haemo- globin Value or Colour Index.	Red Corpuscles per Cubic Millimetre.	White Cor- puscles per Cubic Milli- metre.	Ratio of White to Red Corpuscles.	Percentage of Poly- nuclears.	Lympho- cytes.	Large Mono- nuclears.	Parasites Found.
				°	°									
H.	E.	12	M.	103.0	—	72	0.64	5,620,000	6,875	1-817	68.2	15.6	16.0	Nil.
E. I.		17	M.	98.4	98.4	80	0.79	5,040,000	5,375	1-937	50.4	33.0	16.4	Nil.
H.		32	F.	103.0	103.4	—	—	4,410,000	5,250	1-840	69.0	11.4	19.2	M. T.
H.		30	M.	99.6	101.4	56	0.72	3,910,000	8,250	1-433	66.0	19.2	14.8	Nil.
H.		45	M.	100.8	104.0	68	0.89	3,835,000	4,500	1-852	55.4	36.6	8.0	Nil.
M.		22	M.	97.0	99.0	65	0.71	4,560,000	5,125	1-889	66.4	18.6	14.8	M. T.
M.		21	M.	100.6	104.0	50	0.65	3,825,000	1,275	1-3000	28.6	62.4	13.6	M. T.
M.		21	M.	103.6	103.6	53	0.71	3,745,000	3,875	1-976	35.2	44.0	23.8	M. T.
M.		25	M.	98.6	100.0	51	0.81	3,161,000	5,250	1-602	45.4	27.0	27.4	M. T.
M.		25	M.	105.4	105.4	50	0.97	2,565,000	750	1-3430	66.0	25.8	7.4	M. T.
H.		30	M.	†	†	60	0.73	3,430,000	1,625	1-2111	54.5	25.0	19.6	Nil.
H.		60	M.	101.6	102.6	75	1.15	3,250,000	4,500	1-722	67.6	20.6	11.8	Nil.
N. Ch.		11	F.	†	†	54	0.97	2,790,000	750	1-3720	53.5	40.5	5.0	M. T.
H.		24	M.	104.0	103.0	55	0.98	2,830,000	1,000	1-2830	59.5	11.0	29.0	Nil.
N. Ch.		33	M.	98.0	101.0	24	0.56	2,165,000	1,000	1-2165	39.0	42.0	20.0	Nil.
H.		35	F.	100.6	103.0	22	0.51	2,165,000	1,000	1-2165	48.5	39.0	11.5	M. T.
H.		28	M.	100.4	103.8	38	0.88	2,150,000	2,000	1-1075	26.4	61.4	11.6	Nil.
H.		28	M.	98.2	103.6	39	0.99	1,960,000	3,500	1-560	48.8	38.2	12.6	Nil.
						47	1.22	1,925,000	1,500	1-1283	39.0	46.4	18.8	Nil.
												48.2	12.2	—

* Normal 3 days.

† Normal 5 days.

Normal 1 day.

Degree of Anaemia.—Secondary anaemia, usually of a medium or slight degree, is a well-known result of typhoid fever, and gradually increases in the later stages of the disease. High counts of red cells may be met with as a result of concentration of the blood produced by diarrhoea. Those cases in my table which have been examined more than once show this progressive decrease of both the red corpuscles and the percentage of haemoglobin, the loss having been in proportion to the severity of the cases. In estimating the degree of anaemia it must be remembered that most of the patients were natives, in whom about 70 per cent. of haemoglobin (Gowers's standard) is about the average met with in healthy persons; while in Europeans who have been any length of time in the tropics 70 to 80 per cent. only is commonly found. On the other hand, I have found the number of red corpuscles in health in the tropics to be quite up to the European standard, being usually about 5,000,000, or slightly more, per cubic millimetre. It follows from this that the normal haemoglobin value or colour index will be about 0.7 in a native, and 0.7 to 0.8 in a European not recently arrived in the country. Allowing for these differences from the European standard it will be seen that the haemoglobin is reduced in about the same or in slightly greater proportion than the red corpuscles, the colour index being normal or slightly reduced, having been between 0.6 and 0.8 in the cases tabulated. This is in agreement with the statements of Cabot. The degree of anaemia met with has been comparatively slight, the number of red corpuscles not having fallen below 3,000,000; while it was seldom below 3,500,000 before the end of the third week, by which time there will usually be little doubt about the diagnosis of the case. Further, the haemoglobin seldom falls below 50 per cent. (from a normal of 70 to 80 per cent.). Case No. 8, which is an exception to this rule, had previously suffered from repeated attacks of malarial fever, which was the cause of the greater degree of anaemia. In these cases of typhoid, then, the degree of anaemia was comparatively slight as compared with that often met with in malaria, as will be seen by glancing at Table II.

Total Leucocyte Count.—It is well known that the leucocytes are decreased in both typhoid and malarial fevers, and it is usually stated that no guidance can be obtained from the number met with. This is often so, yet the degree of the decrease may be of diagnostic value in some instances, for in typhoid the white corpuscles are seldom reduced below 3,000 per cubic millimetre and rarely below 2,000. Cabot records only 7 cases out of 491 in which they fell below the latter, and 40 (less than one-tenth) in which they were below the higher one. That is also my experience in persons who have not previously suffered from marked malaria, as was the case with No. 8 in Table I and possibly also with No. 4. On the other hand Table II shows that half the malarial cases gave counts of 2,000 or under, and I have frequently found such

low counts to be distinctly a point in favour of a diagnosis of malaria as against typhoid. In a similar way the proportion of white to red corpuscles in typhoid is but little less than normal, there being seldom much less than 1 white to 1,000 red in cases not complicated by antecedent malaria.

THE BLOOD CHANGES IN MALARIAL REMITTENTS.

Table II shows the blood changes in a series of cases of malarial remittent fever. The temperature at the time the blood was examined is given, as well as the highest temperature recorded within the previous twenty-four hours, so that it can be seen whether the blood was taken during the height of a paroxysm or during a remission. The result of an examination of a specimen stained by Romanowsky's method for the malarial parasite is also noted, from which it will be observed that in several cases they were not found in spite of a careful search, no doubt on account of the quinine having been given freely before the examination. Yet in these cases also the clinical features, temperature charts, progress of the disease, and other blood changes left no doubt as to their being malarial fevers. In every case negative results were obtained by Widal's test for typhoid, and in all that were tested also for Malta fever.

Degree of Anaemia.—The cases have been arranged in accordance with the degree of anaemia met with, beginning with the least and ending with the greatest, as the changes vary somewhat in the different stages. Thus in the first 2 cases no anaemia was present when the examination was made, and in the next 4 the degree is as slight as that often found in typhoid, so that in these cases no help is derived from the degree of anaemia. In the last 5 cases the degree of anaemia is greater than is commonly met with in typhoid, and this may not infrequently be of some diagnostic importance.

High Haemoglobin Value or Colour Index.—Another important point is the high haemoglobin value not infrequently met with in malarial remittents, especially in those cases which present a considerable degree of anaemia. Thus out of the last 8 cases, in which this figure is entered in Table II, 6 show a haemoglobin value considerably above 0.7 (the normal for a native), namely from 0.88 to 1.22, although in the typhoid cases 0.81 is the highest figure recorded. I have elsewhere pointed out that the haemoglobin value may remain high in malaria, although during convalescence the red corpuscles may for a time be replaced quicker than the haemoglobin, and the value may fall, and consequently values lower than normal may sometimes be met with in malarial anaemia. The low value in Case 10 may be accounted for by the patient having suffered from malarial fever for two and a-half months a year before the attack during which the blood count was made, at the beginning of which she showed a chronic enlargement of the spleen and anaemia due to the previous malaria. The haemoglobin value in malarial cases, then, may vary from a

few points below the normal to as many above it, in which respect the disease differs from typhoid with its nearly normal figures. The values above the normal are, I think, of most diagnostic value.

The Total Leucocyte Count.—In malarial remittents with little or no anaemia the total leucocyte count shows only a slight reduction as in typhoid, and is consequently of no help in differentiating the two diseases. On the other hand, in those malarial cases with marked anaemia the total count of white corpuscles is nearly always lower than is commonly met with in typhoid. Counts of below 2,000 per c.mm. are in favour of a diagnosis of malarial as against typhoid fever, while, when only 1,000 or fewer are found, the case has always proved to be malarial in my experience. Further, if the proportion of white to red falls below 1 to 2,000, the case is nearly always malarial or the patient has also suffered fairly recently from that disease to a marked degree.

Parasites.—In every case in which parasites were found they were of the malignant tertian variety, which is the usual form met with in malarial remittents in Calcutta. The cases in which none could be found had been treated with quinine before they were examined by me.

THE DIFFERENTIAL LEUCOCYTE COUNTS IN TYPHOID.

There is a general agreement that the mononuclear leucocytes are increased in uncomplicated cases of typhoid, this change becoming more marked towards the later stages of the disease, and during early convalescence. There appears, however, to be some difference of opinion as to whether it is the small mononuclears (lymphocytes), or the large mononuclears which are found in greater numbers than normal. Thus both Cabot and Coles state that the large mononuclears show the greatest increase; while, on the other hand, Turk's very carefully recorded and complete figures show a marked increase in the small mononuclears, while the large ones are never increased, but more often approach the lower than the upper normal limit, and another observer⁶ has recorded similar counts. When we remember that the line drawn between the small and large mononuclear corpuscles is a purely arbitrary one, which may vary with different workers, such differences of opinion are easily understood, and the necessity of stating exactly how the counts are made is obvious. In health the small mononuclears, averaging according to Cabot 7.5μ , are fairly well defined from the large ones, averaging 13μ , intermediate sizes being comparatively few. When, however, the mononuclears are considerably increased, as in typhoid, then intermediate sizes shading insensibly from the small into the large form are comparatively numerous, and their differentiation correspondingly difficult. In order to get over this difficulty, and to get comparative results in the series of typhoid and malarial remittents respectively, I have adopted the simple expedient of taking advantage of the fact that the average size of the large mononuclears is very nearly that of the polynuclears (13μ to 13.5μ , according to Cabot) and counted all mononuclears, which are distinctly smaller than polynuclears, under the head of lymphocytes, or small mononuclears, and all which were about the same size as, or larger than the polynuclears, as large mononuclears. The closeness with which my figures correspond to those of Turk in each disease lends some support to the correctness of this method, while those who have found the large mononuclears to be increased in typhoid probably counted most of the intermediate sizes under that heading, whereas I should class the majority of them under that of lymphocytes. The division adopted by me has the advantage of simplifying the differentiation of the two forms, as the polynuclears are sufficiently numerous and nearly constant in size to form a convenient standard of comparison, while if the number of large mononuclears is somewhat low this will not affect the comparative value of the figures in the two diseases, in both of which the counts have been made in a similar manner.

The Increase of the Lymphocytes in Typhoid Fever.—In Table I the percentage of the different forms of leucocytes worked out from counts of 500 is given, with the exception of the eosinophiles, which were too few and inconstant in their variations to be of importance. The first two cases well show the gradual change from a nearly normal count at the end of the first week, through a slight increase of the lymphocytes

at the expense of the polynuclears during the second, to a most marked change in the same direction in the later stages of the fever until the lymphocytes may equal or even exceed the polynuclears. In uncomplicated cases this change is remarkably constant, although its appearance may occasionally be delayed, as in Case 5. Moreover, in the cases at the end of the table, in which there was no increase of the lymphocytes, complications such as pneumonia in No. 15, and localized peritonitis in the right iliac fossa due probably to perforation in No. 14, which ended fatally, accounted for the large number of polynuclear leucocytes. In Case 13 also there were marked abdominal symptoms pointing to an exceptional degree of local inflammation, so that the few cases in which the lymphocyte increase is wanting are just those in which as a rule the localizing symptoms of typhoid fever are peculiarly well marked and the diagnosis is not in doubt. On the other hand, in several very mild cases recently examined the lymphocyte increase has been well marked and of great diagnostic value, while I have also seen it in an abortive case with fever for only two weeks, but a strong serum reaction. This lymphocyte increase also persists during the early stages of convalescence, having been found in a well-marked degree as long as five weeks after the termination of a relapse in Case 11, but possibly a late periostitis in this case may have had something to do with its persistence. In another case it was well marked two weeks after the termination of the fever, although at this date the serum reaction was no longer obtainable. Once more this lymphocyte increase has been found well marked in several cases clinically identical with typhoid, but which gave no serum reaction with Widal's test, as is sometimes the case in true typhoid (especially in South Africa, according to recent experience), so that in such cases the corpuscle count may be of great service as a means of confirming the diagnosis. Table I, however, only includes cases which gave the serum reaction. The large mononuclears, on the other hand, were always within the normal limit (4 to 8 according to Cabot, or 3 to 6 as stated by Coles) or were slightly reduced, the figures in my table being very similar to those of Turk,⁵ who records figures ranging from 0.61 to 7.05 per cent., the majority of the cases showing percentages below the mean normal figure, and differing widely in this respect from what is met with in malarial remittents, as will be seen from a glance at Table II.

THE DIFFERENTIAL LEUCOCYTE COUNT IN MALARIAL REMITTENTS.

In Table II the percentages of the different forms of leucocytes in a series of cases of malarial remittents are recorded, the data being arrived at in precisely the same way as in the typhoid fever cases, many of the counts having, indeed, been made before either the serum test or search for malarial parasites had been carried out, with the result that whenever a well-marked lymphocyte increase without any excess of large mononuclears was found, the case proved to be one of typhoid, while whenever a well-marked large mononuclear increase was met with a diagnosis of malaria was correctly indicated. The exact changes, however, depend largely on the degree of temperature and stage of the fever paroxysm when the blood is taken, as well as on the acuteness or chronicity of the case, the degree of anaemia present, and whether the total leucocyte count is slightly or greatly below the normal, so that the figures present a much less degree of uniformity than do those of the typhoid table. It will, therefore, be most convenient to begin with the most constant and important change.

The Increased Percentage of Large Mononuclears.—Every case in the table shows a considerable increase of the large mononuclear corpuscles in some stage of the fever, this increase being most marked during the remissions of the fever or shortly after the temperature has fallen to normal, as already pointed out by Stephens and Christophers.³ In the present series the percentage varied from 11.5 to 29. As a rule, this increase is such a noticeable feature that it can be detected after some practice by a very short inspection of a stained slide with an ordinary high power. It is worthy of note that in Cases 7 and 9, when there was no increase of the large mononuclears during the first examination when the temperature was high, there were other features in the blood changes which served to exclude typhoid and to strongly indicate the

presence of malarial fever. Not only was there a marked degree of anaemia, but the total leucocyte count was below 4,000 per cubic millimetre, and the proportion of white to red corpuscles less than 1 to 3,000, these being figures which we have already seen are very rarely, if ever, met with in typhoid fever, although not very uncommon in malarial fever of long duration. Just, then, in those cases where the increase of the large mononuclears fails, other changes which are of diagnostic value are present, while in the cases which present little anaemia (so that the other blood changes are similar to those which obtain in typhoid) the large mononuclear increase is most marked. The low figure of 8 per cent. at the first count in Case 4 is an exception to this rule. Stephens and Christophers consider that the presence of 15 per cent. or more of large mononuclears is diagnostic of malarial fever, in which opinion I concur, only with the method of counting mentioned above I think the limit might be fixed even lower, such as at about 12 per cent. In the absence of parasites, due generally to previous dosage with quinine, this large mononuclear increase is of the greatest diagnostic value, and can be easily and quickly ascertained from a stained slide.

Presence of Myelocytes.—Another point which has attracted my attention in the present research is the frequency of the occurrence in malarial fevers of very large mononuclear corpuscles with a darkly-stained nucleus and deep blue stained protoplasm with Romanowsky's stain, which appear to be myelocytes. That myelocytes are often present in marked anaemia of malarial origin is mentioned by Cabot, the highest count found by him being 3 per cent. In the tables they are included with the large mononuclear corpuscles, as unfortunately it is only in the most recent cases that they were counted separately, but in the second count in Case No. 6 they formed no less than 5.4 per cent. of the white corpuscles, and in several others from 1 to 3 per cent. of them have been met with. On the other hand, in typhoid an occasional myelocyte has only very rarely been met with in a count of 500 corpuscles. These bodies are so striking that when 2 or 3 per cent. are present they are easily detected on examining a stained slide, and as far as my experience yet goes their presence in these numbers during a continued fever is diagnostic of a malarial remittent, while they may occur in cases with no very marked degree of anaemia. For example, in Case No. 3a with nearly four million red corpuscles, 2.4 per cent. of them were found. If these observations are confirmed by further experience, the presence of myelocytes in any numbers will prove to be of considerable diagnostic value in malarial remittents.

Decrease of Polynuclears and Increase of Lymphocytes.—Lastly, we have to deal with the changes in the proportion of the other leucocytes, namely, the decrease in the polynuclears and a proportionate increase in the lymphocytes. This change is met with in a very variable degree, being most marked as a rule in those cases which present a high degree of anaemia, and least marked or entirely absent in those with little or no anaemia, as illustrated by the first four cases in the table. The increase of the lymphocytes is also most marked in those cases in which the total leucocyte count is lowest, as illustrated by the latter part of the table, but it is just in these that the high degree of anaemia and great proportional decrease in the total number of leucocytes excludes uncomplicated typhoid fever, while the increased percentage of large mononuclears will still be present if malarial fever persists or has only ceased within a few days. On the other hand, I have found a marked increase in the lymphocytes without any excess of large mononuclears in some cases of greatly enlarged spleen, due to malarial cachexia in which no recent fever of a malarious nature has occurred, but these could not possibly be confused with typhoid fever. The extreme decrease of the polynuclears to below 40 per cent. shown in cases, several of the cases in Table II I have only yet met with in chronic malarial fevers.

Leucocytosis.—Although there may be a relative increase in the leucocytes at certain stages of a malarial paroxysm, true leucocytosis very rarely occurs in malaria, not even when it is complicated by broncho-pneumonia, in several cases of which disease I have found a very low leucocyte count in malarial subjects. The presence of marked leucocytosis in cases of intermittent and remittent fevers is, then, of great value in excluding malaria and uncomplicated typhoid fever and

pointing to some form of local inflammation, the most important of which, in my experience in India is liver abscess. On three occasions within the last few months I have found a very high degree of leucocytosis, from 30,000 to 40,000 white corpuscles per cubic millimetre, in cases which were being treated for malaria, and in each case the suspicion of the fever being due to liver abscess thus aroused proved to be correct. Moreover, I have found that the presence of leucocytosis can be detected by a short examination of a stained blood slide, for from twenty to forty white corpuscles may be seen at once in the fields of an ordinary high power all along at the edge of the smear, about 90 per cent. of which will be polynuclears, a condition never met with when the white corpuscles are not increased in numbers, and one which may be taken as evidence of leucocytosis without the necessity of counting the white corpuscles with a haemocytometer.

CONCLUSIONS.

1. The percentage of the different forms of leucocytes counted in a stained blood film is of great diagnostic value in differentiating typhoid and malarial remittent fevers, and is easily ascertained.

2. An increase of the lymphocytes to 40 per cent. or over, without any increase in the large mononuclears, points to typhoid as against malarial fever.

3. An increase in the large mononuclears to about 12 per cent. and upwards, especially during the remissions of the temperature, strongly indicates malaria as against typhoid fever. This change is of great value when parasites are absent from the blood.

4. The presence of myelocytes in any number such as from 1 to 5 per cent. points to malaria as against typhoid fever.

5. A high degree of anaemia, such as a reduction of the red corpuscles to below 3,000,000 per c.mm., is much more frequently met with in malarial than in typhoid fever.

6. A very great reduction in the total leucocyte count, such as to below 2,000 per c.mm., is much more frequently met with in malarial than in typhoid fever, while the proportion of white to red corpuscles in malaria is not infrequently less than 1 to 2,000, which is rare in typhoid fever.

7. Leucocytosis can be detected by the presence of a great excess of white corpuscles, upwards of 80 per cent. of which are polynuclears, in a stained blood film, and is often of service in excluding malaria in intermittent fever due to liver abscess or other local inflammation.

REFERENCES.

¹ Indian Medical Gazette, 1893, p. 176. ² Ibid., 1902. ³ Royal Society's Malaria Committee Reports, Fifth Series, 1901. ⁴ Jour. of Path. and Bact., 1898. ⁵ Klinische Untersuchungen ueber das Verhalten des Blutes bei acuten Infektionskrankheiten.

THE CONDITION OF THE BLOOD IN FILARIASIS.

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ABOUT two years ago Mr. D., a Eurasian student, consulted Dr. Charles Kennedy of this city with regard to a swelling of the left inguinal glands, which was giving him a good deal of pain and discomfort. All the ordinary causes of bubo could with certainty be excluded, and, as the swelling was increasing in size, the patient consented to have the glands excised by Mr. H. J. Stiles. While the operation was being performed a quantity of chylous fluid escaped, and this at once determined the true nature of the case. Some of the fluid was collected and sent to me for examination. I could find no filariae, but it was obvious that the fluid was chyle, and it was resolved to examine the blood in the evening. This was done, and numerous filariae were found. I may remark here that the wound healed by first intention without any further escape of chyle.

In examining stained films of the blood I was struck by the large number of leucocytes in the films, and especially by the high percentage of eosinophiles present. This led me to make a differential count of the leucocytes (films taken on November 28th, 9.20 P.M.), when I found the percentages in 500 cells to be as follows:

